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EXAMINER	
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ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,664	HUANG ET AL.	
	Examiner	Art Unit	
	Dr. Kailash C. Srivastava	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *20040224*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' response filed April 19, 2004 to Office Action mailed November 17, 2003 is acknowledged and entered. The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office action.

CLAIMS STATUS

2. Claims 12-21 have been added.

3. Claims 3-5 and 7 have been amended.

4. Claims 1-21 are pending and are examined on merits.

Information Disclosure Statement

5. Applicants' Information Disclosure (i.e., IDS) filed January 16, 2004 has been made of record and references designated as AL-AN cited therein have been considered.

Priority

6. In response to the benefit granted for the claimed priority date of 09/21/1999, which is the filing date for U.S. Provisional application No. 60/155, 018 under 35 U.S.C. §119 (e), applicants argue that Claims 1-2 and 4-11 should at least be assigned the priority benefit date of 09/20/2000 which is the filing date for the PCT/US00/25733 because the instant U.S. Non-Provisional Application No. 10/088,664 is a National Stage Application for said PCT application under 35 U.S.C. §371.

However, the claims/ claimed subject matter in question presented in referred U.S. non-Provisional application have not been presented in the cited U.S. provisional application, unless applicants can demonstrate to the contrary.

Applicants' arguments regarding the priority benefit rejections have been fully considered but are not persuasive for the reasons of record at page 2, item 5 of the Office Action mailed November 17, 2003 and for additional reasons discussed above.

Claims Objection

7. Claims 3-4, 7-9, 11 and 13-16 are each objected because of the following reasons. Appropriate correction according to Examiner's suggestions is requested.

- The second occurrence of the pronoun "an" in claims 3-4 and 14-15 gives a connotation that the reference is being made to any animal rather than to the same animal that is referred to in the first occurrence of the word, "an". Examiner suggests that to clarify the claimed subject matter and to maintain consistency with claim language in other claims (e.g., Claim 16), applicants replace the second occurrence of the pronoun "an" in Claims 3-4 and 14-15 with the word "the" or the word "said".

- In Claim 7, replacing the word " treatment" with the word "treating" will further clarify said claim.

- In Claim 13, replacing the word " comprises" with the word "comprising" will further clarify said claim.

- In Claim 16 at Line 1, inserting the word --cancer—before the word "or", and word -- of-- before the word cancer will further clarify said claim.

- In Claim 16 at line 2, replacing the word "of" before the word "claim" with the phrase --claimed in-- will further clarify said claim.

- In Claims 8-9 and 11, inserting a --, -- before the word "wherein" is required.

- The subject matter claimed in Claim 18 will be further clear if written as follows: --18. (amended) A pharmaceutical composition as claimed in Claim 12 for treating cancer or reducing the incidence of cancer. --

Claim Rejections - 35 U.S.C. § 112

8. Claims 3-11 and newly presented Claims 12-21 are rejected under 35 U.S.C.§112, first paragraph, because the specification, while enabling for a method to treat cancer via administering a composition comprising a mixture containing all the 14 components of orange peel extract (Specification, Page 4, Line 27 to Page 7, Line 21) or a mixture of tangeritin and nobeletin (Specification page, 7, Line 22 to Page 9, Line 7) or only resveratrol (See Page 12, Line 4 to Page 14, Line 19), does not reasonably provide enablement for a method to prevent cancer via instantly claimed method of administering the instantly claimed pharmaceutical composition comprising orange peel extract/ alleged all 14 components of orange peel extract in mixture with extracts of other plants, other phytochemicals or with resveratrol as claimed. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims because applicants have not demonstrated an example/ examples of entire scope of invention as claimed. Rather, applicants have merely made concluding assertions of their belief (see Page 9, Lines 8-13) that administering mixtures comprising orange peel extract components with a phytochemical compound obtained in extracts from other claimed plant species (e.g., rosemary extract or green tea extract), or with resveratrol/ resveratrol analog in food or dietary or nutraceutical supplements may prevent or treat cancer (e.g., Page 14, Lines 11-19).

Accordingly, undue experimentation without a reasonable expectation of success as to how to determine which combination of orange peel extract or components of orange peel extract with a phytochemical compound in extracts of plants (e.g., Rosemary or Green tea) and/or resveratrol/ resveratrol analog in a physiologically acceptable carrier in which therapeutic amounts of any or all of the claimed designated components would be effective in the instantly claimed method to administer the instantly claimed composition to obtain the instantly claimed functional effect of treating cancer and which type of cancer would be required to practice the invention as claimed due to the quantity of experimentation necessary; limited amount of guidance and limited number of working examples in the specification; nature of the invention; state of the prior art; relative skill level of those in the art; predictability or unpredictability in the art; and breadth of the claims. In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The quantity of undue experimentation would be necessary because applicants have not demonstrated a cumulative/ synergistic effect of claimed compositions/mixtures of claimed components with a pharmaceutical carrier/excipient. There is no guidance in what proportions those components will be mixed and no examples are furnished.

9. In response to rejections to Claims 3-11 and separate rejections to Claims 5, 7, and 10 under 35 U.S.C.§ 112, first paragraph in the Office Action mailed November 17, 2003 Applicants' argue that the enablement rejection is incomplete and further argue that the applicants have data presented at page 4. Line 27 to Page 5, Line 6 enabling the claimed invention with respect to the claimed composition. Applicants' response have been fully considered. Pursuant to the arguments presented and amendments made in applicants' response filed April 19,2004 those rejections are pointless.

10. Claims 1-11 and newly presented Claims 12-21 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Recitation, "extract" in Claims 1-3, 5-6, 12-13 and 20-21 renders those claims vague and unclear because this term, in and of itself, does not adequately delineate its metes and bounds. This term is best defined as a product-by process since product-by-process claims are intended to define products that are otherwise difficult to define (and/or distinguish from the prior art). For example, is the extract obtained by extraction with water, a polar solvent, a non-polar solvent, an acid or base, a squeezed extract, or something else? In addition, from what part(s) of the plant is the extract obtained? It is well accepted in the herbal art that extraction with one of various distinct solvents, as well as from particular parts of therapeutic plants, has a profound impact on the final product with respect to the presence, absence, amounts, and/or ratios of active ingredients therein and, thud, its ability to provide the necessary functional effect(s) instantly claimed and/or disclosed. Since the extract itself is clearly essential to the claimed invention, the steps(s) by which the claimed extract is obtained are also clearly essential and, therefore, must be recited in the claim language itself (i.e., as a product-by-process). Please note that although claims are interpreted in light of the specification, critical limitations from the specification cannot be read into the claims (see, e.g., *In re* Van Guens, 988 F.2d 1181, 26 PSPG2d 1057 (DED. Cir. 1991). Accordingly, without the recitation of all these critical limitations as set forth above, the claims do not adequately define the instant invention. Furthermore, without recitation of limitations as discussed above, an extract is merely a mixture of a variety of components/compounds.

- Recitation, "compound" in Claims 2, 6, 13, 17 and 20 renders those claims unclear, vague and indefinite because an extract of any material without defining conditions to obtain a certain chemical from said extract is a mixture of compounds or non- compound materials (e.g., reaction debris).

- In Claim 5, at Line 3, the word "extract" lacks sufficient antecedent basis because Claim 5 depends from Claim 1, which recites, " a composition comprising an extract". In Claim 1, a composition is claimed not an extract. Extract is merely a component of the claimed composition.

- Claim 19 is rendered vague, unclear and indefinite because of the recitation "Physiologically acceptable carrier or excipient" at both lines 1-2 and at the end of the Claim. Appropriate correction is required.

- While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). The term "physiologically acceptable carrier or excipient in claims 1, 12 and 19 for e.g., is used by the claim to mean " pharmaceutically acceptable carrier or excipient" (See, Osol, A. et al. (eds.) 1980. Remington's Pharmaceutical Sciences. 16th Edition. Philadelphia College of Pharmacy and Science. Pgs. 1256-1260).

- In Claim 21, at Line 3, the word "extract" lacks sufficient antecedent basis because Claim 21 depends from Claim 19, which recites, " a composition".

All other claims depend directly or indirectly from the rejected claims (e.g., Claim 1) and are, therefore, also rejected under 35 U.S.C. §112, second paragraph for the reasons set forth above.

11. In response to rejections to Claims 2, 4 and 6-11 under 35 U.S.C.§ 112, second paragraph in the Office Action mailed November 17, 2003, citing a number of case laws applicants argue that " one skilled in the art would understand the metes and bounds of Claims 2, 4 and 6-11, when read in light of the specification and the teachings of the prior art available to the skilled artisan". Applicants further argue that the term "extract" is a definite term even when used in composition claims in view of the prior art and the status of art" and recite a few patents with term "extract".

Applicants to note that Claims 2, 4 and 6-11 stand rejected under 35 U.S.C.§ 112, second paragraph because even if the details for "extract" and method for obtaining said extract is described in specification, a term can only be read in light of the specification, the language of the specification can not be brought into the claim unless a given claim is documented in said language. Furthermore, even in the Patent examples that applicants cite, the extract has been defined as either alcoholic or ethereal or the extract has been claimed in a claim (e.g., Claim 8, U.S. Patent 6,706,256, "The composition of claim 1 wherein the extract is obtained by solvent extraction and wherein the solvent used for extraction is selected from the group consisting of alcohols, water, acetone, ethyl acetate, glycerol, diethyl ether, propylene glycol and mixtures thereof").

Applicants' response to rejections to Claims 2, 4 and 6-11 under 35 U.S.C.§ 112, second paragraph in the Office Action mailed November 17, 2003, have been fully considered but are not persuasive for the reasons cited above and on pages 4-5, item 10 in the Office Action mailed November 17, 2003.

Claim Rejections – 35 U.S.C. § 102

12. Claims 1, 3, 5, 7-8 and 10-11 are rejected under 35 U.S.C. §102(b) as anticipated by Attaway (Citrus Science and Properties". Food Phytochemicals for Cancer Prevention. ACS Symposia Series, //546. Pp. 240-248) with evidence from Washino et al. (U.S. Patent 5,580,545) and Plant Specimen (http://www.cresentbloom.com /Specimen/CI/default.htm).

Attaway teaches that polymethoxyflavanoids, e.g., tangeritin and nobiletin are more potent tumor cell growth inhibitors and possess anticarcinogenic activities (Abstract, Lines 1-9). Since dry products of fruits, rinds (i.e., peel) or leaf of the members of family Rutaceae are taught to have methooxy and hydroxy flavone compounds (See Washino et al., Abstract and Column 4, Lines 6-9), inherently, Attaway teaches a composition comprising polymethoxyflavanoids in a physiologically acceptable carrier or excipient. Citrus plants, especially *Citrus sinensis* (See applicants' remarks foot note at page 13) are a member of Rutaceae (See Plant Specimen, Pg., 4, entry 7-10). Attaway also teaches anticarcinogenic activity of edible foods (Page 242, Lines 3-6 after Figure 1) and antiproliferative effects of citrus flavonoids to human squamous cell carcinoma "in-vitro" (Page 243, Lines 34-36). Thus, teachings from Attaway clearly show antitumor and anticarcinogenic activities of citrus flavones that are: tangeritin, nobelitin and sinensetin (See Malterud et al., Abstract, Lines 1-4) when administered to humans as an edible food. Thus, Attaway teaches a composition comprising at least three polymethoxylated flavones from orange peel and a method to inhibit tumor cell growth and a method to treat cancer (i.e., squamous cell carcinoma) with a nutraceutical composition comprising citrus flavones.

Therefore, the reference is deemed to anticipate the cited claims.

In this rejection under 35 U.S.C. §102(b), Washino et al. (U.S. Patent 5,580,545) and Plant Specimen (http://www.cresentbloom.com /Specimen/CI/default.htm).
Are respectively cited to merely support that discussed hydroxymethylated flavones are present in citrus peel and that citrus is a member of Rutaceae, and not as a prior art reference.

13. Newly presented Claim 12 is rejected under 35 U.S.C. §102(b) as anticipated by Washino et al. (U.S. Patent 5,580,545) with evidence from Plant Specimen (http://www.cresentbloom.com / Specimen/CI/default.htm).

Washino et al. teach that polymethoxyflavanoids of formula I, are extracted in extracts of dry products of fruits, rinds (i.e., peel) or leaf of the members of family Rutaceae (See, Abstract, Column 2, Lines 12-36 and Column 4, Lines 6-9). Since extracts are finally obtained in a solvent, e.g., water (Column 4, Lines 15-28) and structurally the compounds claimed instantly are same as those taught I the

general formula of Washino et al., inherently, Washino et al., teach a composition comprising polymethoxyflavanoids in a physiologically acceptable carrier or excipient. Furthermore, citrus plants, especially *Citrus sinensis* (See applicants' remarks foot note at page 13) are a member of Rutaceae (See Plant Specimen, Pg., 4, entry 7-10).

Therefore, the reference is deemed to anticipate the cited claim.

In this rejection under 35 U.S.C. §102(b), Plant Specimen (http://www.cresentbloom.com /Specimen/CI/default.htm) is cited to merely support that *Citrus sinensis* is a member of Rutaceae, and not as a prior art reference.

14. In response to art rejections under 35 U.S.C.§ 102(b) to Claims 1.3. 5, 7-8 and 10-11 applicants argue that neither Nagy et al., nor Attaway anticipate the claimed invention, because Nagy et al. teaches a description of flavonoids from citrus fruits and Attaway teaches that citrus polymethoxylated flavonoids nobiletin, tangeritin and sinensetin because according to examiner those materials are obtained from citrus fruits/juice. Applicants further argue that they do not "claim a methoxyflavone per se nor citrus juice, nor even a composition encompassing citrus fruit or a *Citrus* variety in its natural state but instead seeks, in Claim 1, "...an extract of orange3 peel containing three or more polymethoxylated flavones."

In response to applicants' above cited arguments, nobiletin, tangeritin and sinensetin are polymethoxyflavonoids from citrus/orange fruit and peel is a part of the fruit. Applicants' claim is to a composition comprising at least three polymethoxylated flavones. Both Nagy et al. and Attaway teach that composition and Attaway further teaches that said composition has an antiproliferative effects to human squamous cell carcinoma" in vitro".

Applicants' response to rejections to Claims 1, 3, 5, 7-8 and 10-11 under 35 U.S.C.§ 102 (b) in the Office Action mailed November 17, 2003, have been fully considered but are not persuasive for the reasons discussed above and on pages 5-6, items 12-13 in the Office Action mailed November 17, 2003.

Claim Rejections - 35 U.S.C. § 103

15. Claims 1-11 are rejected under 35 U.S.C. § 103 (a) as obvious over Attaway (Citrus Science and Properties". Food Phytochemicals for Cancer Prevention. ACS Symposia Series, //546. Pp. 240-248) with evidence from Washino et al. (U.S. Patent 5,580,545) and Plant Specimen (http://www.cresentbloom.com/Specimen/CI /default.htm) in view of Thomas (U. S. Patent 5,830,738), Peirce (The American Pharmaceutical Association Practical Guide to Natural Medicines, 1999, Stonesong

Press, Inc., Pgs .563-566), Madis Botanicals (Madis Botanicals, Inc., Resverapure™ Resveratrol PE 8%, Product Code 04544, Page 2, Lines 6-7 and 15-31, 1997), Castleman (The Healing Herbs, The Ultimate Guide to the Curative Power of Nature's Medicines, 1991, Rodale Press, Emmaus, PA. Page 349, Column 2, Lines 3-10), and Bailey et al (U.S. Patent 5,859,293).

Claims recite a nutraceutical composition comprising a physiological carrier/excipient, a minimum of three hydroxy flavone obtained from orange peel extract, and at least one other compound among: rosemary extract, Mexican bamboo extract, Huzhang extract, resveratrol, black tea extract, and a hydroxylated or methoxylated resveratrol analog. Claims also recite a method to inhibit tumor cell growth/ treat cancer by administering said composition to an individual in need thereof.

Teachings from Attaway have already been discussed *supra.* Attaway's teachings however, do not disclose the nutraceutical or dietary supplements containing said flavones, with other plant extracts (claimed in Claims 2 and 6) for inhibiting tumor development or reducing the incidence of cancer.

Thomas et al. beneficially teach that carotenoid pigments obtained from orange peels and other plants prevent cancer upon ingestion of these chemicals (Column 1, Lines 22-62). Peirce discloses that rosemary extract helps fight cancer and has been shown to significantly inhibit development of breast cancer (Page 553, Lines 5-7). Bailey et al., (Column1, Lines 29-34 and Column 2, Lines 10-15) and Peirce (Page 553, Lines 5-7) teach inhibition or delayed onset of certain types of cancers when extracts from rosemary and other plants are ingested. Madis Botanicals (Page 2, Column 1, Lines 6-7 and 15-31) teaches powdered nutraceutical and dietary supplement preparations of resveratrol obtained from Huzhang or knotweed to inhibit carcinogenesis or tumerogenesis. Madis Botanicals also discloses that Huzhang or knotweed or Mexican bamboo or giant knotwood are all *Polyganum cuspidatum* and resveratrol is an antioxidant obtained from this plant species. Castleman teaches that black tea has antioxidants and therefore, it may also be helpful in cancer prevention. All the references cited also disclose that the plant extracts cited herein are comprised of antioxidants and it is the antioxidant component of these plants that is effective in either inhibiting or late onset of different types of cancer.

A person of ordinary skill in the art at the time the invention was made would have been motivated to combine the teachings from different prior art references cited *supra* to obtain a pharmaceutical/nutraceutical composition comprising extract from orange peel containing at least three flavones and to administer said pharmaceutical/ nutraceutical composition to an individual in need thereof to treat cancer or inhibit tumor growth; because all of the prior art references (Attaway, Thomas et al., Bailey et al., Peirce and Madis Botanicals) teach inhibition or delayed onset of certain types of cancers when compositions comprising extracts from orange peel, rosemary, Huzhang, Mexican bamboo

and composition containing resveratrol (a compound obtained from Huzhang) are ingested by a mammal in need thereof. While Thomas remedies the deficiency that orange peel extract is anticarcinogenic, Pierce and Bailey et al. remedy the deficiency of rosemary extract having anticarcinogenic property, Castelman remedies the deficiency of the anticarcinogenic property in tea and Madis Botanicals remedies the deficiency of resveratrol or Huzhang, or Mexican bamboo in the teachings from Attaway.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine teachings from all of the prior art references to obtain a nutraceutical/ pharmaceutical composition and to administer said composition to an individual in need thereof to inhibit some types of cancer or tumor growth. Also known in the art are the nutraceutical and dietary supplements of these plant extracts and that ingestion of that composition inhibits tumor growth/cancer. None of the prior art references cited above teach administering said composition in a certain form (e.g., tablet, liquid, or capsule) via inhalation, injection, rectally or vaginally. However, the adjustment of particular conventional working conditions (e.g., mode or form of administration of a composition) is deemed merely a matter of judicious selection and routine optimization of a result-effective parameter that is well within the purview of the skilled artisan.

From the teachings of the cited references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

16. Newly presented Claims 12-21 are rejected under 35 U.S.C. § 103 (a) as obvious over Washino et al. (U.S. Patent 5,580,545) with evidence from and Plant Specimen (http://www.cresentbloom.com/Specimen/CI /default.htm) in view Attaway (Citrus Science and Properties". Food Phytochemicals for Cancer Prevention. ACS Symposia Series, //546. Pp. 240-248) and further in view of Thomas (U. S. Patent 5,830,738), Peirce (The American Pharmaceutical Association Practical Guide to Natural Medicines, 1999, Stonesong Press, Inc., Pgs .563-566), Madis Botanicals (Madis Botanicals, Inc., Resverapure™ Resveratrol PE 8%, Product Code 04544, Page 2, Lines 6-7 and 15-31, 1997), Castleman (The Healing Herbs, The Ultimate Guide to the Curative Power of Nature's Medicines, 1991, Rodale Press, Emmaus, PA. Page 349, Column 2, Lines 3-10), and Bailey et al (U.S. Patent 5,859,293).

Also Claimed is a composition comprising an orange peel extract containing different polymethoxylated flavones and at least one other compound among: rosemary extract, Mexican bamboo extract, Huzhang extract, resveratrol, black tea extract, and a hydroxylated or methoxylated resveratrol

analog. Claims also recite a method to inhibit tumor cell growth/ treat cancer by administering said composition to an individual in need thereof.

Teachings from each one of Washino et al. and / Attaway with evidence from Plant Specimen (http://www.cresentbloom.com/Specimen/CI /default.htm), Thomas, Peirce, Madis Botanicals, Castleman and Bailey et al. have already been discussed *supra.* Subject matter encompassing Claims 12-21 is similar to that of the composition and methods claims 1-11.

A person of ordinary skill in the art at the time the invention was made would have been motivated to combine the teachings from different prior art references cited *supra* to obtain a pharmacetical/nutraceutical composition comprising extract from orange peel containing different polymethoxylated flavones and to administer said pharmaceutical/ nutraceutical composition to an individual in need thereof to treat cancer or inhibit tumor growth; because all of the prior art references (Attaway, Thomas et al., Bailey et al., Peirce and Madis Botanicals) teach inhibition or delayed onset of certain types of cancers when compositions comprising extracts from orange peel, rosemary, Huzhang, Mexican bamboo and composition containing resveratrol (a compound obtained from Huzhang) are ingested by a mammal in need thereof. While Attaway and Thomas remedy the deficiency that orange peel extract is anticarcinogenic, Pierce and Bailey et al. remedy the deficiency of rosemary extract having anticarcinogenic property, Castelman remedies the deficiency of the anticarcinogenic property in tea and Madis Botanicals remedies the deficiency of resveratrol or Huzhang, or Mexican bamboo in the teachings from Washino et al.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine teachings from all of the prior art references to obtain a nutraceutical/ pharmaceutical composition and to administer said composition to an individual in need thereof to inhibit some types of cancer or tumor growth. Also known in the art are the nutraceutical and dietary supplements of these plant extracts and that ingestion of that composition inhibits tumor growth/cancer. None of the prior art references cited above teach administering said composition in a certain form (e.g., tablet, liquid, or capsule) via inhalation, injection, rectally or vaginally. However, the adjustment of particular conventional working conditions (e.g., mode or form of administration of a composition) is deemed merely a matter of judicious selection and routine optimization of a result-effective parameter that is well within the purview of the skilled artisan.

Furthermore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the instant ingredients for their known benefit since each is well known in the art for the same purpose and for the following reasons. This rejection is based on the well

established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman,* 1943 C.D. 518. Applicants invention is predicated on an unexpected result, which typically involves synergism, an unpredictable phenomenon, highly dependent upon specific proportions and/or amounts of particular ingredients. Any mixture of the components embraced by the claims which does not exhibit an unexpected result (e.g., synergism) is therefore *ipso facto* unpatentable.

Accordingly, the instant claims, in the range of proportions where no unexpected results are observed, would have been obvious to one of ordinary skill having the above-cited references before him.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

17. In response to the rejections to Claims 1-11 in Office Action November 17, 2003, applicants argue that the claimed invention is unobvious over the cited references, because the cited references do not disclose or suggest, or provide motivation to arrive at the presently claimed invention.

Applicants' arguments regarding rejections to Claims 1-11 under 35 U.S.C.§103(a) in Office Action mailed November 17, 2003 have been fully considered but are not deemed to be persuasive because of the above cited discussion and reasons of record at pages 6-8 of the Office Action cited *supra.*

In response to applicants' arguments against the references individually, one cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller,* 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicants' argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine,* 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones,* 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, those reasons have been discussed above and also cited at pages 6-8 of the Office Action cited *supra.* Furthermore, a rejection under 35 U.S.C. § 103 (a) based upon the combination of references is not deficient solely because the references are

combined based upon a reason or technical consideration which is different from that which resulted in the claimed invention (*Ex parte Raychem Corp*, 17 U.S.P.Q. 2d 1417).

CONCLUSION

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. No Claims are allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:30 A.M. to 6:00 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (571) 272-0926 Monday through Thursday. The fax phone number for the organization where this application or proceeding is assigned is (703)-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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RALPH GITOMER
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July 12, 2004